

Supplementary Methods

Protocol for the purification of live alpha-, beta-, and delta-cell from mouse islets

Day -1

- Mouse islet isolation
- Islet purification by handpicking
- Overnight culture for recovery in RPMI 1640 + 10% (vol/vol) FBS

Day 0

- Evaluate islets microscopically to ensure they look healthy
- Staining of islets for FACS
 - o Collect islets in a 15ml tube
 - o Centrifuge 5min at 280g to pellet the islets and remove supernatant
 - o Add 1ml of 50% Trypsin (0.5ml trypsin + 0.5ml HBSS Ca⁻/Mg⁻)
 - o Vortex 3s and incubate for 3min at 37°C
 - o Vortex 3s and check for tissue rests (e.g. sedimentation of intact islets)
 - o Add 2ml of FACS medium (HBSS Ca⁻/Mg⁻, Phenol Red, 10% FCS)
 - o Centrifuge 5min at 515g to pellet the cells and remove supernatant as much as possible
 - o Prepare mix of antibodies for FACS staining in 100ul of FACS medium
 - a-TER199-PerCP-Cy5.5, 1/100
 - a-CD31-PerCP-Cy5.5, 1/100
 - a-CD45-PerCP-Cy5.5, 1/200
 - a-EPCAM-BV605, 1/100
 - a-CD24-APC-Fire750, 1/100
 - a-CD133-APC, 1/200
 - a-CD71-FITC, 1/100
 - a-CD49f-PE, 1/100
 - o Incubate 15min at 4°C
 - o Add 1ml of FACS medium
 - o Centrifuge 5min at 515g to pellet the cells and remove supernatant
 - o Resuspend in FACS medium with propidium iodide (1/4000).
- Pass stained cells from the 15ml tube through the filter-top of a 5ml FACS tube and keep them on ice until FACS
- FACS gating method (for the above mix of antibodies)
 - o Exclude debris and select cells of interest using FSC-A vs SSC-A
 - o Select singlets using FSC-H vs FSC-W
 - o Select lineage negative cells using PerCP-Cy5.5-A
 - o Select epithelial EPCAM⁺ cells using BV605-A
 - o Gate both the CD24^{high} and the CD24^{low} subsets using APC-Fire750-A
 - Within the CD24^{high} subset select the CD49f cells using PE-A, this fraction contains the delta cells (CD24^{high} CD49f)
 - Within the CD24^{low} subset select the CD71⁻ and CD71⁺ cells using PE-A vs FITC, these fractions contain the alpha-cells (CD24^{low} CD71⁻) and beta-cells (CD24^{low} CD71⁺), respectively.

Cell recovery upon sorting is around 80% for the Epcam⁺ cells as measured by propidium iodide staining.

Average yield of purified cells per 100 mouse islets: 6000 CD24^{low}CD71⁺ (beta-enriched fraction), 1500 CD24^{low}CD71⁻ (alpha-enriched fraction) and 700 CD24^{high}CD49f (delta-enriched fraction).

Supplementary Figure 1.

(a) Flow cytometry plots of dispersed islet-cells from adult C57BL/6 mice, as described in Figure 1a. Top panels show the gating strategy for obtaining the live Lin⁻EpCam⁺ fraction. Bottom panels show intracellular staining of insulin and glucagon in the CD24^{high} fraction within Lin⁻EpCam⁺ cells. Plots are representative of 3 independent experiments; each experiment is a pool of 4 to 12 mice. **(b)** Relative mRNA expression of the exocrine genes *Cpa1* and *Sox9* and **(c)** the endocrine genes *Ins1*, *Gcg*, and *Sst* in the sorted subsets CD24^{high}CD49f⁺ (black), CD24^{high}CD49f (red), CD24^{low}CD71⁺ (blue), and CD24^{low}CD71⁻ (purple). **(d)** Flow cytometry plots of dispersed islets from adult C57BL/6 mice after conjugated-transferrin (TF-CF568) incorporation. Left panel shows CD24 and CD71 expression in the EpCam⁺ fraction, middle panel shows TF-CF568 fluorescence and right panel shows CD71 expression in EpCam⁺CD24^{high} fraction. **(e)** TF-CF568 fluorescence on CD24^{low} CD71⁺ (blue), CD71⁻ (purple) and CD24^{high} (red) epithelial cells. One-way ANOVA. Full lines indicate mean, error bars for s.e.m. Data are representative of 3 independent experiments.

Supplementary Figure 2.

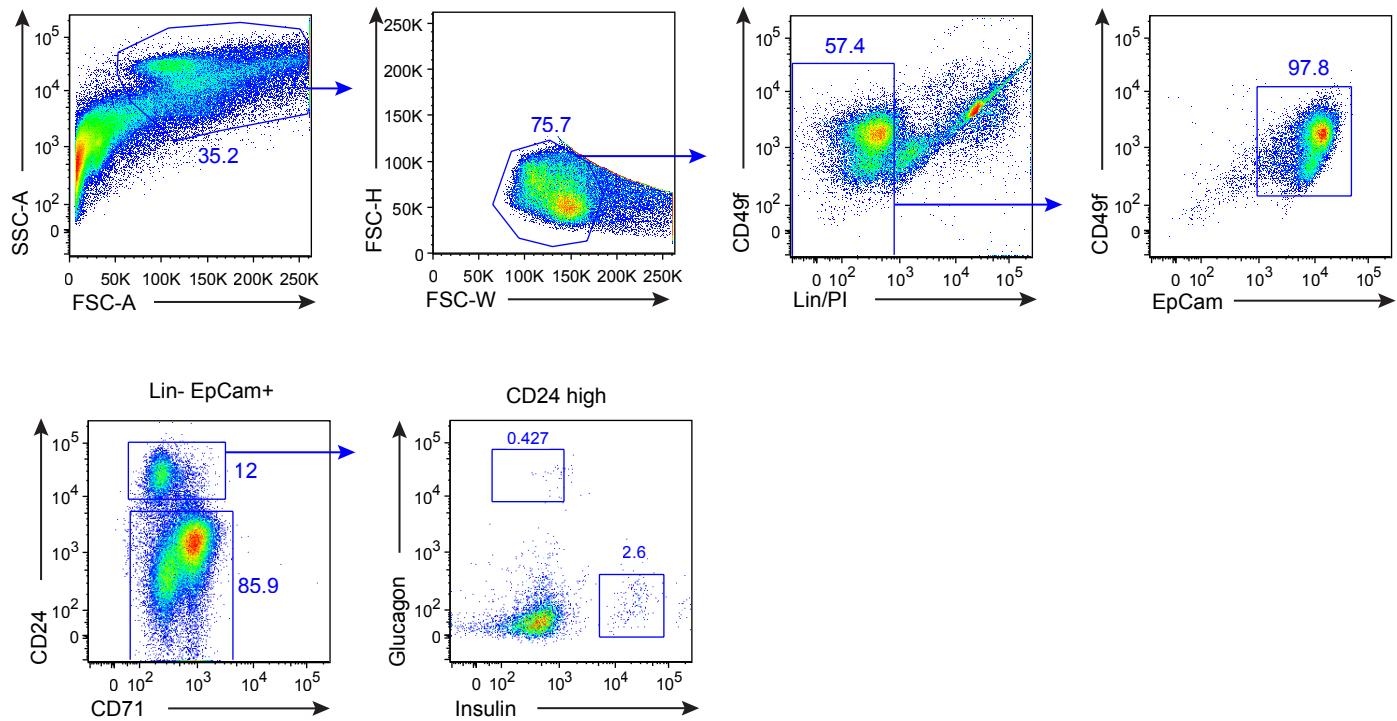
(a) Flow cytometry plots of dispersed fetal pancreas (FP) cells from C57BL/6 pups at embryonic day (E)14.5. Top panels show the gating strategy for obtaining the live Lin⁻EpCam⁺ fraction. Bottom panel shows the staining for CD49f and CD133 which allows the separation of 3 subsets as described previously by Sugiyama et al. (2007). **(b)** Flow cytometry plots of dispersed FP from C57BL/6 pups at E14.5, E16.5, and E18.5 showing the relative frequency of fraction I, II and III defined by CD49f and CD133 expression within the live Lin⁻EpCam⁺ fraction.

Supplementary Figure 3.

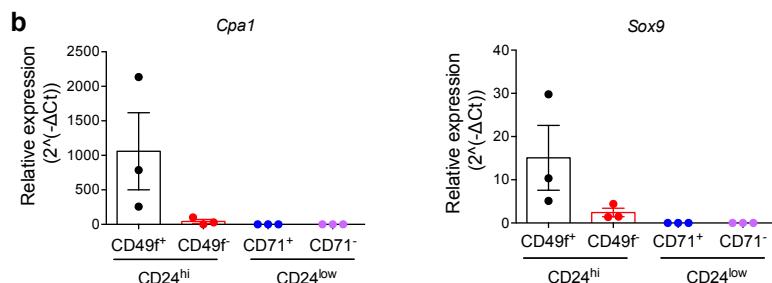
(a) Quality control of RNAseq analysis confirming low expression of lineage (*Pecam1*, *Ptprc*, *Ter119*) and mesenchymal (*Vim*) transcripts in all sorted subsets. **(b)** Transcript levels of surface markers used for cell sorting *Epcam*, *Cd24a*, *Itga6*, and *Tfrc* in all sorted subsets. Data from RNAseq analysis, gene expression in RSEM. Full lines indicate mean, error bars for s.e.m. ND: not detected. **(c)** Comparison of the relative abundance of selected transcripts in sorted α -, β -, and δ -cells between an approach that uses hormone-reporter mice (DiGruccio et al. [2016]) and the current report using surface markers. Expression levels are normalized per dataset to the mean expression level in the cell type with highest transcript abundance, *Ins1* and *Ins2* were normalized to the β -cell subset, *Gcg* to the α -cell subset, and *Sst* to the δ -cell subset.

Supplementary figure 1

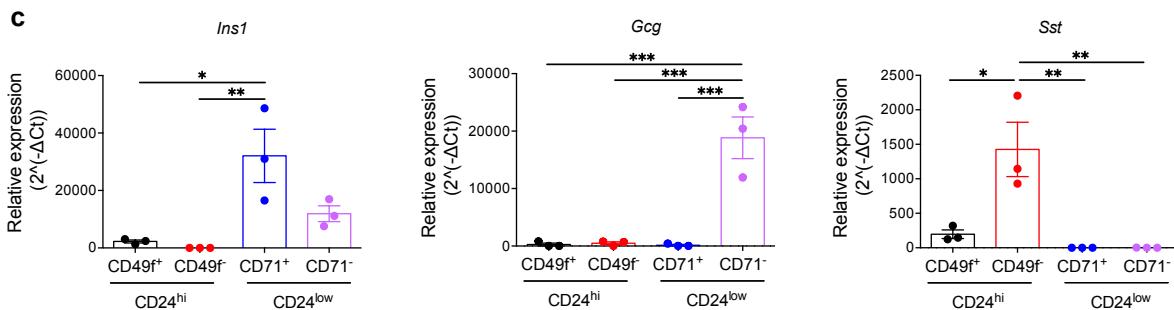
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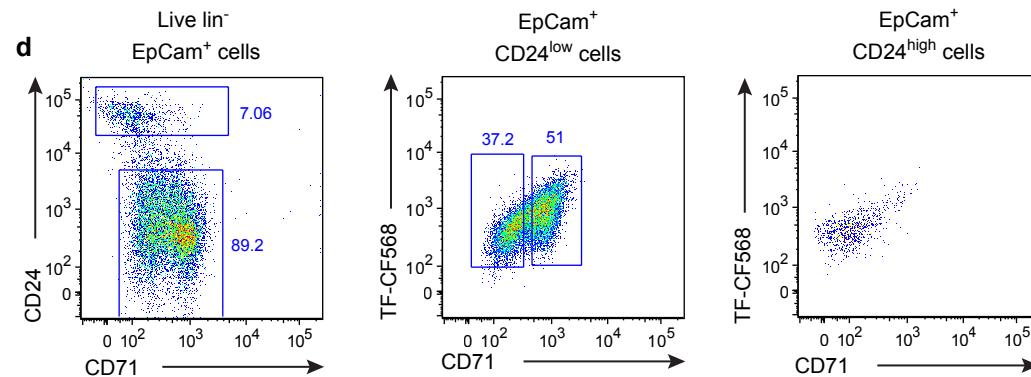
b



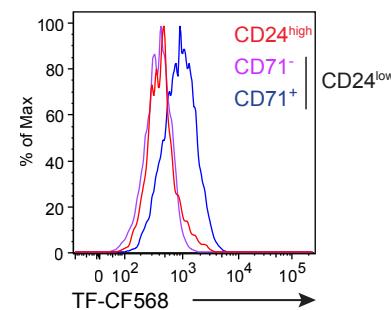
c



d

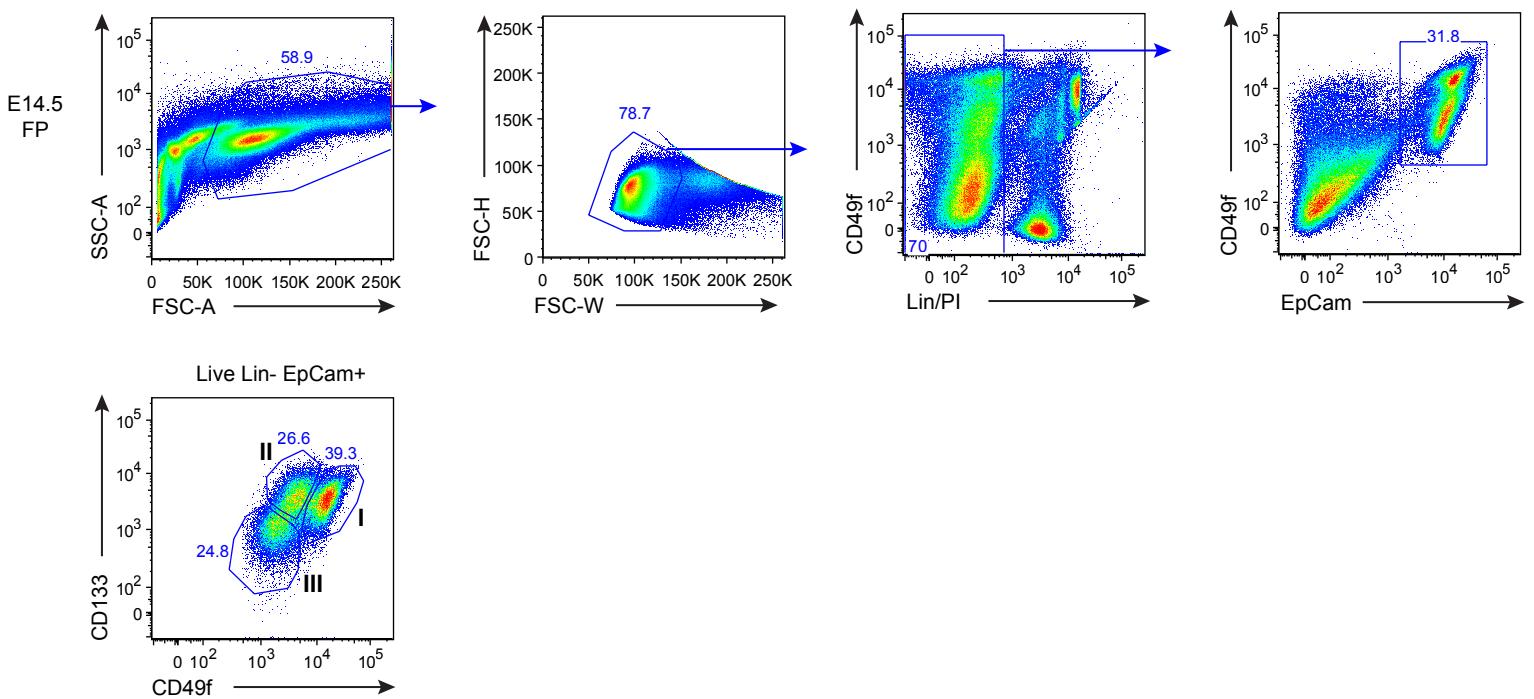


e

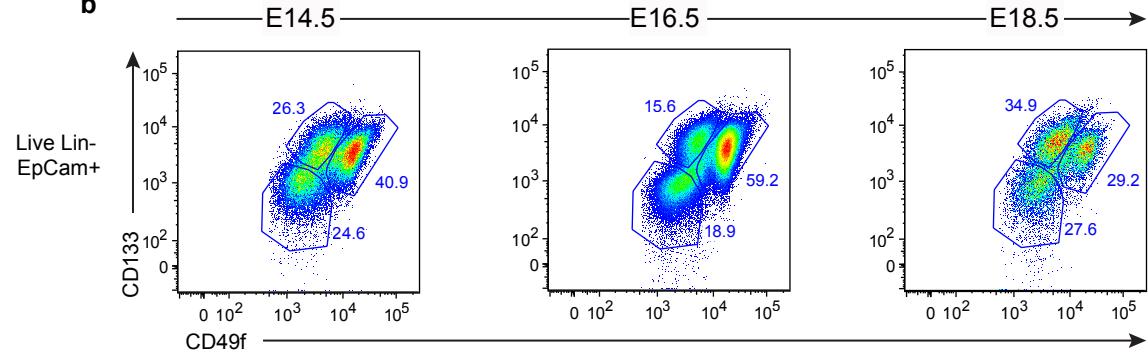


Supplementary figure 2

a

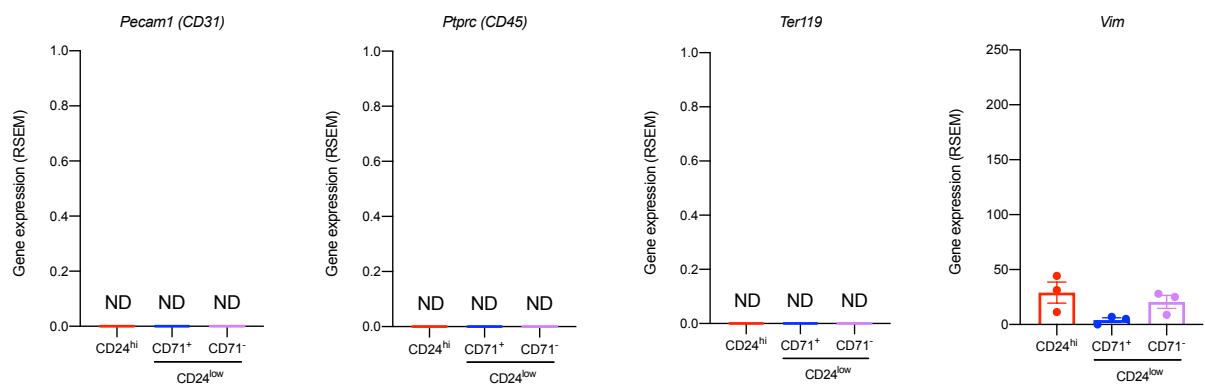


b

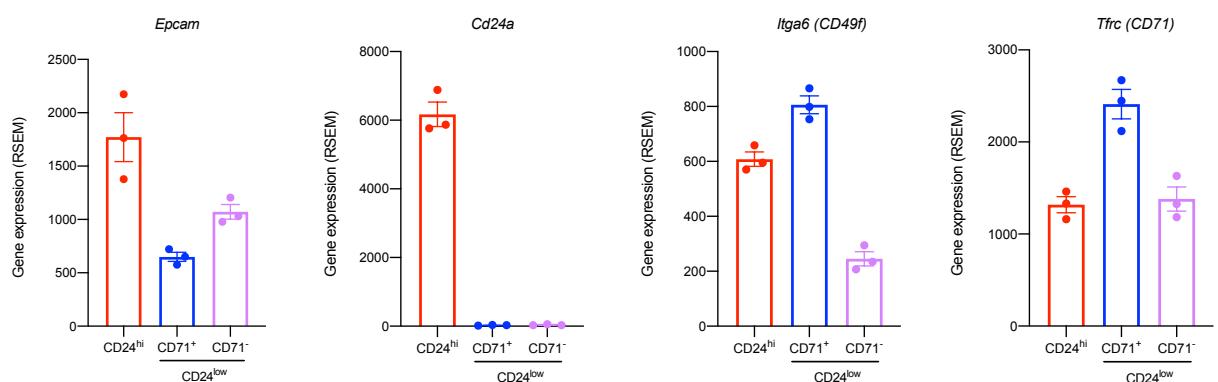


Supplementary figure 3

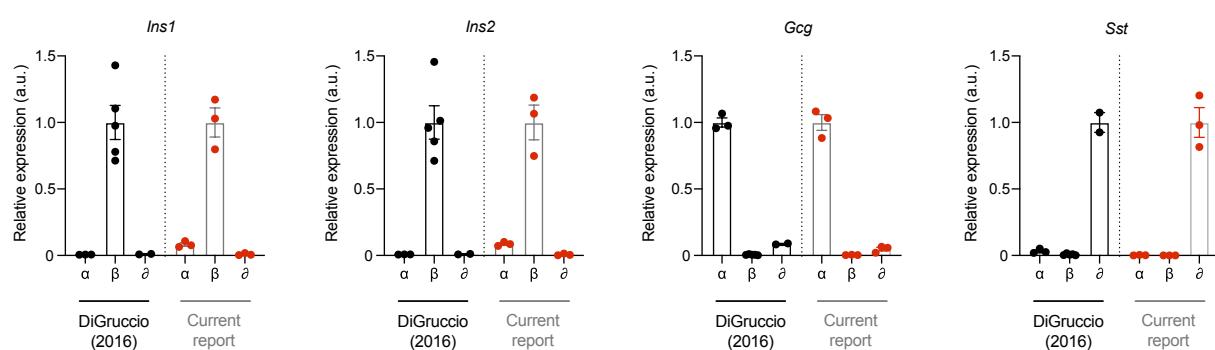
a



b



c



Supplementary table 1. List of antibodies

Target	Clone	Conjugation	Catalog N°	Company	Application	Dilution
EpCam	G8.8	BV605	BLE118227	Biolegend	FACS	1/100
		BV421	BLE118225			
CD31	MEC13.3	PercPCy5.5	BLE102522	Biolegend	FACS	1/100
CD45	30-F11	PercPCy5.5	BLE103132	Biolegend	FACS	1/200
CD24	MA/69	APC-Fire 750	BLE101840	Biolegend	FACS	1/100
CD49f	GoH3	PE	BLE313612	Biolegend	FACS	1/200
CD71	RI7217	FITC	BLE113806	Biolegend	FACS	1/100
CD71	CY1G4	FITC	BLE334104	Biolegend	FACS	1/50
CD133	315-2C11	APC	BLE141208	Biolegend	FACS	1/200
Insulin	C27C9	AF-647	#9008	Cell Signaling Technologies	FACS	1/100
	Polyclonal	Not conjugated	20056		IHC	1/1000
Glucagon	U16-850	BV421	565891	BD Biosciences	FACS	1/200
	Polyclonal	Not conjugated	20076		IHC	1/1000
Somatostatin	Polyclonal	Not conjugated	A0566	Immunostar	IHC	1/200
TER-119	TER-119	PercPCy5.5	BLE116228	Biolegend	FACS	1/100

Supplementary table 2. Oligonucleotides used for qPCR

RefSeq ID	Gene	Oligonucleotide	Sequence	Amplicon length (bp)
NM_025350	<i>Cpa1</i>	Mm-Cpa/fw	GGAGGAGTTGGAGCACTTGA	110
		Mm-Cpa/rv	AGAATGCTTCACGGACTGG	
NM_008100	<i>Gcg</i>	Mm-Gcg/fw	TGAAGACAAACGCCACTCAC	132
		Mm-Gcg/rv	TGACGTTGGCAATGTTGTT	
NM_010491	<i>Iapp</i>	Mm-Iapp/fw Mm-Iapp/rv		
NM_008386	<i>Ins1</i>	Mm-Ins1/fw	CAGAGACCATCAGCAAGCAG	133
		Mm-Ins1/rv	GGGACCACAAAGATGCTGTT	
NM_144955	<i>Nkx6-1</i>	Mm-Nkx6-1/fw	CCCGGAGTGATGCAGAGT	127
		Mm-Nkx6-1/rv	TTTGCTGTCCAGAGAACGTG	
NM_194350	<i>Mafa</i>	Mm-Mafa/fw	TTCAGCAAGGAGGAGGTCAT	134
		Mm-Mafa/rv	CTCTGGAGCTGGCACTTCTC	
NM_008814	<i>Pdx1</i>	Mm-Pdx1/fw	GAAATCCACCAAAGCTCACG	95
		Mm-Pdx1/rv	TGTAGGCAGTACGGGTCTCTC	
NM_008907	<i>Ppia</i>	Mm-Ppia/fw	CAGGTCCTGGCATCTTGTCC	187
		Mm-Ppia/rv	TGCTTGCTGGCTTGCATTCC	
NM_011448	<i>Sox9</i>	Mm-Sox9/fw	AGGAAGCTGGCAGACCAGTA	107
		Mm-Sox9/rv	TCCACGAAGGGTCTTCTC	
NM_009215	<i>Sst</i>	Mm-Sst/fw	TCCGTCAGTTCTGCAGAAGTCTC	62
		Mm-Sst/rv	GTACTTGGCCAGTTCTGTTCCC	
NM_011638	<i>Tfrc</i>	Mm-Tfrc/fw	CTGTAGAGGCCTTCCTAGT	99
		Mm-Tfrc/rv	ATGACAATGGTTCCCCACCAA	

Supplementary table 3. TaqMan assays used for qPCR

RefSeq ID	Gene	Assay ID	Amplicon length (bp)
NM_007693	<i>Chga</i>	Mm00514341_m1	59
NM_008100	<i>Gcg</i>	Mm00801714_m1	85
NM_013556	<i>Hprt</i>	Mm03024075_m1	113
NM_008386	<i>Ins1</i>	Mm01950294_s1	80
NM_008907	<i>Ppia</i>	Mm02342430_g1	148
NM_031197	<i>Slc2a2</i>	Mm00446224_m1	83
NM_009215	<i>Sst</i>	Mm00436671_m1	86
NM_025350	<i>Cpa1</i>	Mm00465942_m1	78
NM_011448	<i>Sox9</i>	Mm00448840_m1	101

Supplementary table 4. Gene set enrichment analysis of RNAseq from sorted beta-cells compared with alpha-cells. Results for the “GO Response to Iron Ion” gene set as visualized in Fig 6b.

	Probe	Description	Rank in gene list	Rank metric score	Running ES	Core enrichment
1	PDX1	pancreatic and duodenal homeobox 1 [Source:HGNC Symbol;Acc:HGNC:6107]	33	4,131	0,140	Yes
2	ABAT	4-aminobutyrate aminotransferase [Source:HGNC Symbol;Acc:HGNC:23]	399	2,271	0,189	Yes
3	ATP7A	ATPase copper transporting alpha [Source:HGNC Symbol;Acc:HGNC:869]	452	2,140	0,259	Yes
4	G6PD	glucose-6-phosphate dehydrogenase [Source:HGNC Symbol;Acc:HGNC:4057]	844	1,523	0,280	Yes
5	CCND1	cyclin D1 [Source:HGNC Symbol;Acc:HGNC:1582]	1037	1,346	0,311	Yes
6	HFE	homeostatic iron regulator [Source:HGNC Symbol;Acc:HGNC:4886]	1123	1,279	0,348	Yes
7	SNCA	synuclein alpha [Source:HGNC Symbol;Acc:HGNC:11138]	1154	1,260	0,389	Yes
8	HMOX1	heme oxygenase 1 [Source:HGNC Symbol;Acc:HGNC:5013]	1181	1,242	0,430	Yes
9	IREB2	iron responsive element binding protein 2 [Source:HGNC Symbol;Acc:HGNC:6115]	1495	1,034	0,440	Yes
10	B2M	beta-2-microglobulin [Source:HGNC Symbol;Acc:HGNC:914]	1620	0,976	0,464	Yes
11	CCNB1	cyclin B1 [Source:HGNC Symbol;Acc:HGNC:1579]	2429	0,684	0,423	No
12	ACO1	aconitase 1 [Source:HGNC Symbol;Acc:HGNC:117]	3105	0,516	0,386	No
13	BMP6	bone morphogenetic protein 6 [Source:HGNC Symbol;Acc:HGNC:1073]	4230	0,295	0,306	No
14	BECN1	beclin 1 [Source:HGNC Symbol;Acc:HGNC:1034]	4851	0,193	0,263	No
15	MDM2	MDM2 proto-oncogene [Source:HGNC Symbol;Acc:HGNC:6973]	5790	0,040	0,189	No
16	ALAD	aminolevulinate dehydratase [Source:HGNC Symbol;Acc:HGNC:395]	6055	0,004	0,168	No
17	DRD2	dopamine receptor D2 [Source:HGNC Symbol;Acc:HGNC:3023]	6080	0	0,166	No
18	SLC11A2	solute carrier family 11 member 2 [Source:HGNC Symbol;Acc:HGNC:10908]	6926	-0,116	0,102	No
19	C1QA	complement C1q A chain [Source:HGNC Symbol;Acc:HGNC:1241]	7454	-0,190	0,066	No
20	FXN	frataxin [Source:HGNC Symbol;Acc:HGNC:3951]	7582	-0,208	0,063	No
21	APBB1	amyloid beta precursor protein binding family B member 1 [Source:HGNC Symbol;Acc:HGNC:581]	7775	-0,236	0,056	No
22	HIF1A	hypoxia inducible factor 1 subunit alpha [Source:HGNC Symbol;Acc:HGNC:4910]	9264	-0,481	-0,0470	No
23	MAP1LC3A	microtubule associated protein 1 light chain 3 alpha [Source:HGNC Symbol;Acc:HGNC:6838]	9905	-0,621	-0,077	No
24	SLC40A1	solute carrier family 40 member 1 [Source:HGNC Symbol;Acc:HGNC:10909]	11751	-1,653	-0,168	No
25	TF	transferrin [Source:HGNC Symbol;Acc:HGNC:11740]	11979	-2,119	-0,113	No
26	BCL2	BCL2 apoptosis regulator [Source:HGNC Symbol;Acc:HGNC:990]	12391	-4,428	0,006	No

Supplementary table 5. Gene set enrichment analysis of RNAseq from sorted beta-cells compared with alpha-cells. Results for the “GO Iron Ion Transport” gene set as visualized in Fig 6c.

	Probe	Description	Rank in gene list	Rank metric score	Running ES	Core enrichment
1	NECTIN1	nectin cell adhesion molecule 1 [Source:HGNC Symbol;Acc:HGNC:9706]	230	2,849	0,045	Yes
2	MELTF	melanotransferrin [Source:HGNC Symbol;Acc:HGNC:7037]	242	2,763	0,105	Yes
3	ATP7A	ATPase copper transporting alpha ferritin light chain [Source:HGNC Symbol;Acc:HGNC:869]	452	2,140	0,136	Yes
4	FTL	ATPase H ⁺ transporting V1 subunit A [Source:HGNC Symbol;Acc:HGNC:3999]	539	1,961	0,173	Yes
5	ATP6V1A	ATPase H ⁺ transporting V0 subunit A1 transferrin receptor [Source:HGNC Symbol;Acc:HGNC:851]	611	1,822	0,208	Yes
6	TFRC	ATPase H ⁺ transporting V0 subunit e1 [Source:HGNC Symbol;Acc:HGNC:11763]	1020	1,360	0,205	Yes
7	ATP6V0E1	ATPase H ⁺ transporting V0 subunit e1 homeostatic iron regulator [Source:HGNC Symbol;Acc:HGNC:863]	1073	1,321	0,230	Yes
8	HFE	ATPase H ⁺ transporting V1 subunit E1 [Source:HGNC Symbol;Acc:HGNC:4886]	1123	1,279	0,255	Yes
9	ATP6V1E1	ATPase H ⁺ transporting V1 subunit E1 [Source:HGNC Symbol;Acc:HGNC:857]	1236	1,192	0,272	Yes
1	ATP6V0A2	ATPase H ⁺ transporting V0 subunit a2 [Source:HGNC Symbol;Acc:HGNC:18481]	1288	1,157	0,294	Yes
1	STEAP2	STEAP2 metalloreductase [Source:HGNC Symbol;Acc:HGNC:17885]	1381	1,095	0,311	Yes
1	IREB2	iron responsive element binding protein 2 [Source:HGNC Symbol;Acc:HGNC:6115]	1495	1,034	0,325	Yes
1	TTYH1	tweety family member 1 [Source:HGNC Symbol;Acc:HGNC:13476]	1582	0,995	0,340	Yes
1	ATP6V0C	ATPase H ⁺ transporting V0 subunit c [Source:HGNC Symbol;Acc:HGNC:855]	1611	0,982	0,360	Yes
1	B2M	beta-2-microglobulin [Source:HGNC Symbol;Acc:HGNC:914]	1620	0,976	0,381	Yes
1	ATP6V1D	ATPase H ⁺ transporting V1 subunit D [Source:HGNC Symbol;Acc:HGNC:13527]	1840	0,887	0,383	Yes
1	ATP6V1G	ATPase H ⁺ transporting V1 subunit G1 [Source:HGNC Symbol;Acc:HGNC:864]	1852	0,880	0,402	Yes
1	DNM2	dynamin 2 [Source:HGNC Symbol;Acc:HGNC:2974]	2153	0,773	0,395	No
1	CLTC	clathrin heavy chain [Source:HGNC Symbol;Acc:HGNC:2092]	2448	0,678	0,386	No
2	MMGT1	membrane magnesium transporter 1 [Source:HGNC Symbol;Acc:HGNC:28100]	2476	0,671	0,399	No
2	RAB11B	RAB11B, member RAS oncogene family [Source:HGNC Symbol;Acc:HGNC:9761]	3048	0,528	0,365	No
2	STEAP3	STEAP3 metalloreductase [Source:HGNC Symbol;Acc:HGNC:24592]	3134	0,509	0,369	No
2	ATP6V1G	ATPase H ⁺ transporting V1 subunit G2 [Source:HGNC Symbol;Acc:HGNC:862]	3276	0,476	0,368	No
2	ATP6V0D1	ATPase H ⁺ transporting V0 subunit d1 [Source:HGNC Symbol;Acc:HGNC:13724]	3280	0,474	0,379	No
2	ABCB7	ATP binding cassette subfamily B member 7 [Source:HGNC Symbol;Acc:HGNC:48]	3329	0,464	0,385	No
2	SLC25A37	solute carrier family 25 member 37 [Source:HGNC Symbol;Acc:HGNC:29786]	3636	0,406	0,369	No
2	SLC25A28	solute carrier family 25 member 28 [Source:HGNC Symbol;Acc:HGNC:23472]	3911	0,353	0,355	No
2	ATP6V0A1	ATPase H ⁺ transporting V0 subunit a1 [Source:HGNC Symbol;Acc:HGNC:865]	3970	0,342	0,358	No
2	ATP6V0B	ATPase H ⁺ transporting V0 subunit b [Source:HGNC Symbol;Acc:HGNC:861]	4071	0,325	0,357	No
3	ARHGAP1	Rho GTPase activating protein 1 [Source:HGNC]	4092	0,322	0,363	No

0		Symbol;Acc:HGNC:673]					
3	ATP6V1B2	ATPase H+ transporting V1 subunit B2 [Source:HGNC Symbol;Acc:HGNC:854]	4135	0,314	0,367	No	
3		ATPase H+ transporting V1 subunit C1					
2	ATP6V1C1	[Source:HGNC Symbol;Acc:HGNC:856]	4547	0,245	0,339	No	
3		sideroflexin 1 [Source:HGNC					
3	SFXN1	Symbol;Acc:HGNC:16085]	4636	0,228	0,337	No	
3		lipocalin 2 [Source:HGNC					
4	LCN2	Symbol;Acc:HGNC:6526]	4817	0,198	0,327	No	
3		ceruloplasmin [Source:HGNC					
5	CP	Symbol;Acc:HGNC:2295]	4836	0,195	0,330	No	
3		lemur tyrosine kinase 2 [Source:HGNC					
6	LMTK2	Symbol;Acc:HGNC:17880]	5055	0,159	0,316	No	
3		ATPase H+ transporting V0 subunit e2					
7	ATP6V0E2	[Source:HGNC Symbol;Acc:HGNC:21723]	5120	0,150	0,314	No	
3		ATPase H+ transporting accessory protein 1					
8	ATP6AP1	[Source:HGNC Symbol;Acc:HGNC:868]	5598	0,071	0,277	No	
3		ATPase H+ transporting V1 subunit F					
9	ATP6V1F	[Source:HGNC Symbol;Acc:HGNC:16832]	6097	-0,002	0,237	No	
4		ATPase H+ transporting V1 subunit H					
0	ATP6V1H	[Source:HGNC Symbol;Acc:HGNC:18303]	6210	-0,016	0,228	No	
4		solute carrier family 48 member 1					
1	SLC48A1	[Source:HGNC Symbol;Acc:HGNC:26035]	6406	-0,042	0,213	No	
4		mucolipin 1 [Source:HGNC					
2	MCOLN1	Symbol;Acc:HGNC:13356]	6777	-0,094	0,186	No	
4		solute carrier family 11 member 2					
3	SLC11A2	[Source:HGNC Symbol;Acc:HGNC:10908]	6926	-0,116	0,176	No	
4		feline leukemia virus subgroup C cellular					
4	FLVCR2	receptor family member 2 [Source:HGNC Symbol;Acc:HGNC:20105]	9370	-0,501	-0,009	No	
4		ATP binding cassette subfamily B member 6					
5	ABCB6	(Langereis blood group) [Source:HGNC Symbol;Acc:HGNC:47]	9426	-0,509	-0,002	No	
4		solute carrier family 22 member 17					
6	SLC22A17	[Source:HGNC Symbol;Acc:HGNC:23095]	10145	-0,685	-0,045	No	
4		solute carrier family 46 member 1					
7	SLC46A1	[Source:HGNC Symbol;Acc:HGNC:30521]	10225	-0,706	-0,036	No	
4		phosphatidylinositol binding clathrin assembly					
8	PICALM	protein [Source:HGNC Symbol;Acc:HGNC:15514]	10457	-0,777	-0,037	No	
4		STEAP4 metalloreductase [Source:HGNC					
9	STEAP4	Symbol;Acc:HGNC:21923]	10799	-0,893	-0,044	No	
5		T cell immune regulator 1, ATPase H+					
0	TCIRG1	transporting V0 subunit a3 [Source:HGNC Symbol;Acc:HGNC:11647]	10874	-0,923	-0,030	No	
5		feline leukemia virus subgroup C cellular					
1	FLVCR1	receptor 1 [Source:HGNC Symbol;Acc:HGNC:24682]	10967	-0,958	-0,016	No	
5		solute carrier family 39 member 14					
2	SLC39A14	[Source:HGNC Symbol;Acc:HGNC:20858]	11156	-1,068	-0,007	No	
5		RAB15 effector protein [Source:HGNC					
3	REP15	Symbol;Acc:HGNC:33748]	11460	-1,306	-0,003	No	
5		solute carrier family 40 member 1					
4	SLC40A1	[Source:HGNC Symbol;Acc:HGNC:10909]	11751	-1,653	0,011	No	
5		transferrin [Source:HGNC					
5	TF	Symbol;Acc:HGNC:11740]	11979	-2,119	0,040	No	

Supplementary table 6. Gene set enrichment analysis of RNAseq from sorted beta-cells compared with alpha-cells. Results for the “Reactome Iron Uptake and Transport” gene set as visualized in Fig 6d.

Probe	Description	Rank in gene list	Rank metric score	Running ES	Core enrichment
1 FTL	ferritin light chain [Source:HGNC Symbol;Acc:HGNC:3999]	539	1,961	0,018	Yes
2 ATP6V1A	ATPase H+ transporting V1 subunit A [Source:HGNC Symbol;Acc:HGNC:851]	611	1,822	0,069	Yes
3 TFRC	transferrin receptor [Source:HGNC Symbol;Acc:HGNC:11763]	1020	1,360	0,078	Yes
4 ATP6V0E1	ATPase H+ transporting V0 subunit e1 [Source:HGNC Symbol;Acc:HGNC:863]	1073	1,321	0,115	Yes
5 HFE	homeostatic iron regulator [Source:HGNC Symbol;Acc:HGNC:4886]	1123	1,279	0,151	Yes
6 HMOX1	heme oxygenase 1 [Source:HGNC Symbol;Acc:HGNC:5013]	1181	1,242	0,185	Yes
7 ATP6V1E1	ATPase H+ transporting V1 subunit E1 [Source:HGNC Symbol;Acc:HGNC:857]	1236	1,192	0,218	Yes
8 ATP6V0A2	ATPase H+ transporting V0 subunit a2 [Source:HGNC Symbol;Acc:HGNC:18481]	1288	1,157	0,250	Yes
9 UBC	ubiquitin C [Source:HGNC Symbol;Acc:HGNC:12468]	1291	1,156	0,286	Yes
10 STEAP2	STEAP2 metalloreductase [Source:HGNC Symbol;Acc:HGNC:17885]	1381	1,095	0,312	Yes
11 IREB2	iron responsive element binding protein 2 [Source:HGNC Symbol;Acc:HGNC:6115]	1495	1,034	0,336	Yes
12 ATP6V0C	ATPase H+ transporting V0 subunit c [Source:HGNC Symbol;Acc:HGNC:855]	1611	0,982	0,357	Yes
13 ATP6V1D	ATPase H+ transporting V1 subunit D [Source:HGNC Symbol;Acc:HGNC:13527]	1840	0,887	0,366	Yes
14 ATP6V1G1	ATPase H+ transporting V1 subunit G1 [Source:HGNC Symbol;Acc:HGNC:864]	1852	0,880	0,393	Yes
15 HMOX2	heme oxygenase 2 [Source:HGNC Symbol;Acc:HGNC:5014]	2418	0,686	0,369	No
16 ACO1	aconitase 1 [Source:HGNC Symbol;Acc:HGNC:117]	3105	0,516	0,329	No
17 STEAP3	STEAP3 metalloreductase [Source:HGNC Symbol;Acc:HGNC:24592]	3134	0,509	0,343	No
18 ATP6V1G2	ATPase H+ transporting V1 subunit G2 [Source:HGNC Symbol;Acc:HGNC:862]	3276	0,476	0,346	No
19 ATP6V0D1	ATPase H+ transporting V0 subunit d1 [Source:HGNC Symbol;Acc:HGNC:13724]	3280	0,474	0,361	No
20 UBB	ubiquitin B [Source:HGNC Symbol;Acc:HGNC:12463]	3882	0,357	0,324	No
21 ATP6V0A1	ATPase H+ transporting V0 subunit a1 [Source:HGNC Symbol;Acc:HGNC:865]	3970	0,342	0,327	No
22 ATP6V0B	ATPase H+ transporting V0 subunit b [Source:HGNC Symbol;Acc:HGNC:861]	4071	0,325	0,329	No
23 ATP6V1B2	ATPase H+ transporting V1 subunit B2 [Source:HGNC Symbol;Acc:HGNC:854]	4135	0,314	0,334	No
24 ATP6V1C1	ATPase H+ transporting V1 subunit C1 [Source:HGNC Symbol;Acc:HGNC:856]	4547	0,245	0,309	No
25 LCN2	lipocalin 2 [Source:HGNC Symbol;Acc:HGNC:6526]	4817	0,198	0,293	No
26 CP	ceruloplasmin [Source:HGNC Symbol;Acc:HGNC:2295]	4836	0,195	0,298	No
27 CAND1	cullin associated and neddylation dissociated 1 [Source:HGNC Symbol;Acc:HGNC:30688]	5060	0,159	0,285	No
28 ATP6V0E2	ATPase H+ transporting V0 subunit e2 [Source:HGNC Symbol;Acc:HGNC:21723]	5120	0,150	0,285	No
29 ATP6AP1	ATPase H+ transporting accessory protein 1 [Source:HGNC Symbol;Acc:HGNC:868]	5598	0,071	0,248	No

30	ATP6V1F	ATPase H+ transporting V1 subunit F [Source:HGNC Symbol;Acc:HGNC:16832]	6097	-0,002	0,208	No
31	ATP6V1H	ATPase H+ transporting V1 subunit H [Source:HGNC Symbol;Acc:HGNC:18303]	6210	-0,016	0,200	No
32	SKP1	S-phase kinase associated protein 1 [Source:HGNC Symbol;Acc:HGNC:10899]	6542	-0,062	0,175	No
33	CUL1	cullin 1 [Source:HGNC Symbol;Acc:HGNC:2551]	6708	-0,083	0,165	No
34	MCOLN1	mucolipin 1 [Source:HGNC Symbol;Acc:HGNC:13356]	6777	-0,094	0,162	No
35	FBXL5	F-box and leucine rich repeat protein 5 [Source:HGNC Symbol;Acc:HGNC:13602]	6811	-0,099	0,162	No
36	SLC11A2	solute carrier family 11 member 2 [Source:HGNC Symbol;Acc:HGNC:10908]	6926	-0,116	0,157	No
37	UBA52	ubiquitin A-52 residue ribosomal protein fusion product 1 [Source:HGNC Symbol;Acc:HGNC:12458]	9604	-0,547	-0,042	No
38	SLC22A17	solute carrier family 22 member 17 [Source:HGNC Symbol;Acc:HGNC:23095]	10145	-0,685	-0,064	No
39	SLC46A1	solute carrier family 46 member 1 [Source:HGNC Symbol;Acc:HGNC:30521]	10225	-0,706	-0,048	No
40	NEDD8	neural precursor cell expressed, developmentally down-regulated 8 [Source:HGNC Symbol;Acc:HGNC:7732]	10476	-0,784	-0,044	No
41	GLRX3	glutaredoxin 3 [Source:HGNC Symbol;Acc:HGNC:15987]	10809	-0,897	-0,043	No
42	TCIRG1	T cell immune regulator 1, ATPase H+ transporting V0 subunit a3 [Source:HGNC Symbol;Acc:HGNC:11647]	10874	-0,923	-0,019	No
43	FLVCR1	feline leukemia virus subgroup C cellular receptor 1 [Source:HGNC Symbol;Acc:HGNC:24682]	10967	-0,958	0,003	No
44	SLC40A1	solute carrier family 40 member 1 [Source:HGNC Symbol;Acc:HGNC:10909]	11751	-1,653	-0,008	No
45	TF	transferrin [Source:HGNC Symbol;Acc:HGNC:11740]	11979	-2,119	0,040	No